

PCT/GB 03/03376

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C07D237/24	C07D237/08	C07D237/20	C07D237/14	C07D401/10
	C07D405/10	C07D403/10	C07D403/12	C07D401/12	C07D409/04
	C07D401/04	C07D405/14	C07D409/14	C07D401/14	C07D417/14

According to International Patent Classification (IPC) or to both national classification and IPC

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) :

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal, WPI Data, BIOSIS

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02 38568 A (HALLETT DAVID JAMES ;MERCK SHARP & DOHME (GB); RUSSELL MICHAEL GEO) 16 May 2002 (2002-05-16) example 93 claim 13 ----	1,10,11
X	WO 02 22605 A (KNEGTEL RONALD ;BEBBINGTON DAVID (GB); CHARRIER JEAN DAMIEN (GB);) 21 March 2002 (2002-03-21) Table 7, examples VIII-1, VIII-14, VIII-33 ----	1,10
X	EP 0 072 726 A (SANOFI SA) 23 February 1983 (1983-02-23) table I ----	1,10,13
	----- -/-	

**X** ~ Further documents are listed in the continuation of box C:

**X** Patent family members are listed in annex.

<sup>a</sup> Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the International search report

16 October 2003

03/11/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

**Fanni, S**

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/03376

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D403/04 A61K31/4965 A61K31/497

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WERMUTH, CAMILLE GEORGES ET AL:  "Synthesis and structure-activity relationships of a series of aminopyridazine derivatives of gamma.-aminobutyric acid acting as selective GABA-A antagonists"  JOURNAL OF MEDICINAL CHEMISTRY (1987), 30(2), 239-49,  XP002257939  Scheme I, compound III;  Scheme II, compound 9a</p> <p style="text-align: center;">-/--</p>	1

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

16 October 2003

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Fann1, S

## INTERNATIONAL SEARCH REPORT

PCT/GB 03/03376

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AURICCHIO, SERGIO ET AL: "New cleavage of the azirine ring by single electron transfer: the synthesis of 2H-imidazoles, pyridazines and pyrrolines" EUROPEAN JOURNAL OF ORGANIC CHEMISTRY (2001), (6), 1183-1187, XP002257940 examples 3A-3C	1
X	RIVAL, YVELINE ET AL: "5-HT3 Antagonists Derived from Aminopyridazine-type Muscarinic M1 Agonist" JOURNAL OF MEDICINAL CHEMISTRY (1998), 41(3), 311-317, XP002257941 scheme 1	1,10
X	SOUTH, MICHAEL S. ET AL: "Synthesis and Reactions of Haloazodienes. A New and General Synthesis of Substituted Pyridazines" JOURNAL OF ORGANIC CHEMISTRY (1996), 61(25), 8921-8934, XP002257942 examples 9,10; table 1	1
X	BLY, RUTA K. ET AL: "Heterocyclic studies. XIII. The aldol condensation of 2,3-dihydro-5-methy 6-phenyl-4H-1,2diazepin-4-one and rearrangement to a pyridazine" JOURNAL OF ORGANIC CHEMISTRY (1964), 29(8), 2128-35, XP002257943 examples 15A-D	1
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ATKINSON, C. M. ET AL: "Triazaphenanthrenes. III. Synthesis of some 9-aryl-2,3,10- triazaphenanthrenes" retrieved from STN Database accession no. 53:67737 XP002257945 abstract & JOURNAL OF THE CHEMICAL SOCIETY, ABSTRACTS (1959) 1-5,	1
	--- -/-	

## INTERNATIONAL SEARCH REPORT

PCT/GP 03/03376

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CA 'Online!            CHEMICAL ABSTRACTS SERVICE, COLUMBUS,            OHIO, US;            SAMSONOV, V. A. ET AL: "Preparation and            reactions of pyrroline N-oxides obtained            by reaction of isonitroso ketones with            enamines"            retrieved from STN            Database accession no. 126:18740            XP002257946            abstract            &amp; KHIMIYA GETEROTSIKLICHESKIKH SOEDINENII            (1996), (8), 1055-1061,</p>	1
X	<p>HARRIS, R.L.N. ET AL.: "The effect of            C-2-carboxyphenyl Derivatives of Certain            Heterocyclic Compounds on Root Geotropism            in Cress Seedlings"            PESTICIDE SCIENCE,            vol. 11, 1980, pages 439-444, XP009019048            example XV</p>	1
X	<p>OLIVER, J.E ET AL.: "Alkylation and            Rearrangement of Lithiated            3-Methyl-1,2-benzisoxazoles"            JOURNAL OF ORGANIC CHEMISTRY,            vol. 54, 1989, pages 4970-4973,            XP002257944            table I</p>	1
X	<p>BREUKELMAN, S.P: "Preparation and some            Reactions of 4- and            5-Aryl-4,5-dihydropyrazin-3(2H)-ones"            J. CHEM. SOC. PERKIN TRANS.,            1985, pages 1627-1635, XP009019047            page 1629; example 25</p>	1
X	<p>JOJMA, T. ET AL.: "Pyridazine I. Novel            Intramolecular Cycloaddition of            3-Chloro-6-(2-allylphenoxy)pyridazines"            CHEMICAL&amp;PHARMACEUTICAL BULLETIN,            vol. 20, no. 10, - 1972 pages 2191-2203,            XP009019056            page 2195; example IX</p>	1
X	<p>US 4 810 705 A (CHAMBON JEAN-PIERRE ET            AL) 7 March 1989 (1989-03-07)            examples I-IX</p>	1
A	<p>US 6 255 305 B1 (GUIBLIN ALEXANDER RICHARD            ET AL) 3 July 2001 (2001-07-03)            column 3, line 4 - line 18            claim 1</p>	1,10,13

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/03376

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 13  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 1 (partially)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 13 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 13

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 1(partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to compounds of formula I according to present claim 1 for which R1 is always other than hydrogen.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

PCT/EP 03/03376

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0238568	A	16-05-2002	AU 1253002 A	21-05-2002
			CA 2427779 A1	16-05-2002
			EP 1343788 A1	17-09-2003
			WO 0238568 A1	16-05-2002
			WO 03008418 A1	30-01-2003
			US 2003055060 A1	20-03-2003
WO 0222605	A	21-03-2002	AU 9091201 A	26-03-2002
			AU 9091401 A	26-03-2002
			AU 9094401 A	26-03-2002
			AU 9101301 A	26-03-2002
			AU 9267001 A	26-03-2002
			AU 9455801 A	26-03-2002
			AU 9687101 A	26-03-2002
			AU 9687501 A	26-03-2002
			BR 0114088 A	17-06-2003
			CA 2422299 A1	21-03-2002
			CA 2422354 A1	21-03-2002
			CA 2422367 A1	21-03-2002
			CA 2422371 A1	21-03-2002
			CA 2422377 A1	21-03-2002
			CA 2422378 A1	21-03-2002
			CA 2422379 A1	21-03-2002
			CA 2422380 A1	21-03-2002
			EP 1317447 A1	11-06-2003
			EP 1317444 A1	11-06-2003
			EP 1317448 A1	11-06-2003
			EP 1318997 A1	18-06-2003
			EP 1317449 A1	11-06-2003
			EP 1317450 A1	11-06-2003
			EP 1317452 A1	11-06-2003
			EP 1318814 A2	18-06-2003
			HU 0302172 A2	29-09-2003
			HU 0302173 A2	29-09-2003
			NO 20031188 A	13-05-2003
			NO 20031189 A	13-05-2003
			NO 20031190 A	13-05-2003
			NO 20031191 A	13-05-2003
			WO 0222603 A1	21-03-2002
			WO 0222601 A1	21-03-2002
			WO 0222604 A1	21-03-2002
			WO 0222605 A1	21-03-2002
			WO 0222606 A1	21-03-2002
			WO 0222607 A1	21-03-2002
			WO 0222608 A1	21-03-2002
			WO 0222602 A2	21-03-2002
			US 2003073687 A1	17-04-2003
			US 2003083327 A1	01-05-2003
			US 2003064981 A1	03-04-2003
			US 2003064982 A1	03-04-2003
			US 2003055044 A1	20-03-2003
			US 2003078166 A1	24-04-2003
			AU 3116602 A	01-07-2002
			AU 3404702 A	01-07-2002
			BR 0116493 A	30-09-2003
			CA 2432129 A1	25-07-2002
EP 0072726	A	23-02-1983	FR 2510998 A1	11-02-1983

## INTERNATIONAL SEARCH REPORT

PCT/GP 03/03376

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0072726	A	AR 231441 A1	30-11-1984
		AR 231637 A1	31-01-1985
		AT 18216 T	15-03-1986
		AT 12227 T	15-04-1985
		AU 548930 B2	09-01-1986
		AU 8655382 A	10-02-1983
		AU 548931 B2	09-01-1986
		AU 8655482 A	10-02-1983
		CA 1174240 A1	11-09-1984
		CA 1179346 A1	11-12-1984
		CS 229940 B2	16-07-1984
		CS 229941 B2	16-07-1984
		DD 202715 A5	28-09-1983
		DD 202549 A5	21-09-1983
		DE 3262671 D1	25-04-1985
		DE 3269383 D1	03-04-1986
		DK 354382 A ,B,	08-02-1983
		DK 354482 A ,B,	08-02-1983
		EG 15788 A	30-09-1986
		EG 15747 A	30-06-1986
		EP 0074863 A1	23-03-1983
		EP 0072726 A1	23-02-1983
		ES 8305737 A1	16-07-1983
		ES 8305738 A1	16-07-1983
		FI 822747 A ,B,	08-02-1983
		FI 822748 A ,B,	08-02-1983
		GR 76429 A1	10-08-1984
		GR 76430 A1	10-08-1984
		HU 189166 B	30-06-1986
		HU 190028 B	28-08-1986
		IE 53387 B1	26-10-1988
		IE 53388 B1	26-10-1988
		IL 66408 A	31-12-1985
		IL 66409 A	29-09-1985
		JP 1771027 C	30-06-1993
		JP 4059312 B	21-09-1992
		JP 58077867 A	11-05-1983
		JP 58077868 A	11-05-1983
		KR 8901569 B1	08-05-1989
		KR 8801624 B1	02-09-1988
		NO 822509 A ,B,	08-02-1983
		NO 822510 A ,B,	08-02-1983
		NZ 201518 A	30-04-1985
		NZ 201520 A	30-04-1985
		OA 7175 A	30-04-1984
		OA 7176 A	30-04-1984
		PH 18545 A	09-08-1985
		PL 237808 A1	28-02-1983
		PL 237809 A1	28-02-1983
US 4810705	A	FR 2562071 A1	04-10-1985
		CA 1249276 A1	24-01-1989
		EP 0156734 A2	02-10-1985
		JP 60224691 A	09-11-1985
US 6255305	B1	AT 236904 T	15-04-2003
		AU 724076 B2	14-09-2000
		AU 3551997 A	20-02-1998



# INTERNATIONAL SEARCH REPORT

PCT/GB 03/03376

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6255305	B1	AU 723098 B2	17-08-2000
		AU 3553997 A	20-02-1998
		BG 103112 A	30-09-1999
		BR 9710729 A	17-08-1999
		CA 2260774 A1	05-02-1998
		CN 1251589 A	26-04-2000
		CZ 9900181 A3	16-06-1999
		DE 69720732 D1	15-05-2003
		EA 2436 B1	25-04-2002
		EE 9900027 A	16-08-1999
		EP 0915877 A1	19-05-1999
		EP 0915875 A2	19-05-1999
		WO 9804560 A1	05-02-1998
		WO 9804559 A2	05-02-1998
		JP 2002514169 T	14-05-2002
		JP 2000515851 T	28-11-2000
		KR 2000029548 A	25-05-2000
		NO 990304 A	25-03-1999
		NZ 333768 A	29-09-2000
		PL 331072 A1	21-06-1999
		SK 9399 A3	10-04-2000
		TR 9900047 T2	22-03-1999
		US 6465462 B1	15-10-2002
		ZA 9706591 A	18-08-1998
		HR 980035 A1	30-06-1999
		TW 480261 B	21-03-2002